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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,941	08/09/2001	John R. Stuelpnagel	A-67616-4/RMS/DCF/SRN	6890

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EXAMINER

FORMAN, BETTY J

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 12/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center">Office Action Summary</p>	Application No. 09/925,941	Applicant(s) STUELPNAGEL ET AL.	
	Examiner BJ Forman	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 6-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
 a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u>11/05</u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 16 September 2003 in which claims 2-4, 6 and 10 were amended and claim 5 was canceled. And supplemental Response filed 21 November 2003. All of the amendments have been thoroughly reviewed and entered.

The previous objections and rejections under 35 U.S.C. 112, second paragraph in the Office Action dated 18 March 2003 are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 102(e) and 35 U.S.C. 103(a) are maintained.

All of the arguments have been thoroughly reviewed and are discussed below. New grounds for rejection are discussed.

Claims 1-4 and 6-10 are under prosecution.

Priority

2. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. The Provisional Application filed 9 February 1999 upon which priority is claimed does not provide adequate support under 35 U.S.C. 112 for claims 1-4 of this application because the provisional application does not teach or describe the instantly claimed "mapping a grid". The provisional application teaches incorporating fiducials into the assay structure to control alignment of the structure (page 22, lines 4-10) wherein the fiducials define an edge, stripe or have an orientation which allows translation of the images detected (page 23, lines 10-17). And the provisional application describes a fiducial template which is created from various images

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of the array (page 23, lines 18-32). But the provisional application does not teach or describe the instantly claimed mapping a grid.

Provisional Application filed 9 February 1999 upon which priority is claimed does not provide adequate support under 35 U.S.C. 112 for claims 5-10 of this application because the provisional application does not teach or describe the instantly claimed “determining the similarity of a first signal from at least one discrete site to at least one reference signal” and “comparing said first signal to a threshold similarity measure obtained by comparing a reference signal to a theoretical signal” (Claims 6-10).

Because the provisional application does not provide support for the instant claims, the effective filing date for instant claims 1-4 & 6-10 is the filing date of parent application 09500,555 i.e. 9 February 2000.

Response to Arguments

3. Applicant argues that support for “mapping a grid” is found in the provisional application at page 23, lines 29-33 and page 24, lines 1-2 wherein a method is described for obtaining or generating a fiducial template that can be mapped onto each data image. Applicant further states that the provisional application teaches use of “image pro” software for generating template images which is the same software used in the 09/500,555 application for mapping a grid.

Applicant’s arguments have been considered but are not found persuasive because while the ’555 application does teach the instantly claimed “mapping a grid”, the fact that the provisional application uses the same software as the ’555 application, does not illustrate that the software was used to map a grid as instantly claimed. The fact that the “image pro” software was used in provisional application and the ’555 application, merely illustrates that the “image pro” software can be used both for generating a fiducial template and for mapping a grid. The cited passage is provided below. Nowhere in the passage is a grid or mapping a grid

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described. As such, the effective filing date for the instant claims is the filing date of the '555 application i.e. 02/09/2000.

Once these "registration" images are collected, they can then be used to build a template using standard image processing software such as image Pro (Media Cybernetics). This type of software allows the user to create simultaneous software segments to calculate the mean pixel intensity over region of interest using a simple, one step segmentation function. This software-based fiducial template can then be mapped onto each data image in the assay protocol to allow data collection for each region for each data image. See for example U.S. Patent No. 5,768,412 This allows the location of each array feature or pixel to be defined.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-4 are rejected under 35 U.S.C. 102(e) as being anticipated by Walt et al (U.S. Patent No. 6,327,410 B1, filed 11 September 1998).

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Regarding Claim 1, Walt et al disclose a method of determining the presence of a target analyte in a sample comprising acquiring a first data image (i.e. optical signature) of a random array composition comprising a substrate with a surface comprising discrete sites and a population of microspheres comprising at least a first and a second subpopulation each comprising a bioactive agent wherein said microspheres are distributed on said surface such that each of said discrete sites contain no more than one microsphere (Column 3, lines 35-45; Column 5, line 61-Column 6, line 29; and Fig. 5 & 7) mapping a grid (i.e. matrices) onto said first data image to create a registered first data image (i.e. optical signature) contacting said random array with a sample, acquiring a second data image from said array with said sample, mapping a grid (matrices) onto said second data image to create a registered second data image and comparing first and second registered data image to determine the presence or absence of said target analyte (Column 18, line 59-Column 19, line 53; Column 27, lines 30-50; and Fig. 10).

Regarding Claim 2, Walt et al disclose the method wherein said discrete sites are wells (Column 6, lines 22-29).

Regarding Claim 3, Walt et al disclose the method wherein said bioactive agents are proteins (Column 8, lines 50-59).

Regarding Claim 4, Walt et al disclose the method wherein said bioactive agents are nucleic acids (Column 9, lines 41-50).

Response to Arguments

6. Applicant argues that Walt et al create matrices to determine the location of each bead in the array, but do not teach mapping a grid onto the first data image to create a registered data image as instantly claimed. The argument has been considered but is not found persuasive because Walt et al specifically teach creating a first matrix to obtain a first optical signature and creating a second matrix to obtain a second optical signature and further comparing the optical signatures (using the matrix)(Column 19, lines 31-53). The instant

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claims are drawn to mapping a grid to create a first and a second registered data image. The phrase "mapping a grid" clearly encompasses the matrix creation of Walt et al because a matrix is generally defined as "a rectangular array of elements arranged in rows and columns" (Ninth New Collegiate Dictionary, Merriam-Webster, page 733). Therefore, given the broadest reasonable interpretation of the claims, Walt et al disclose the claimed invention.

The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 6-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al (U.S. Patent No. 6,327,410 B1, filed 11 September 1998) in view of Lockhart et al (U.S. Patent No. 6,040,138, filed 15 September 1995).

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Regarding Claims 6-10, Walt et al disclose a signal preprocessing comprising acquiring a first data image (i.e. optical signature) of a random array composition comprising a substrate with a surface comprising discrete sites and a population of microspheres comprising at least a first and a second subpopulation each comprising a bioactive agent wherein said microspheres are distributed on said surface such that each of said discrete sites contain microspheres (Column 3, lines 35-45; Column 5, line 61-Column 6, line 29; and Fig. 5 & 7) determining the similarity of a first signal from at least one discrete site to at least one reference signal wherein when said first signal is similar to at least one of said reference signals, said discrete site contains a bead (Column 19, lines 31-53). Walt et al compare a first signal and second signal to determine bead presence (Column 19, lines 46-53) which clearly suggests that they compare the signal to a threshold signal (e.g. first signal) to determine presence of the bead. Additionally, signal detection and comparison to a threshold measure was well known in the art at the time the claimed invention was made as taught by Lockhart et al who teach a similar method of signal processing. The method of Lockhart et al comprises acquiring a first data image of the array (i.e. signal intensities of the control sample on the array) wherein the array comprises a substrate with a surface comprising discrete sites bioactive agent and obtaining a first signal from a discrete site and comparing the signal to a threshold measure (threshold intensity value) to thereby determine the presence of a bioactive agent at the site (Column 23, line 41-Column 24, line 6) whereby a true signal is distinguished from a background signal. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the threshold measure of Lockhart et al to the signal detection and comparison of Walt et al to thereby determine presence or absence of a bead, to discard a signal below the threshold and to accurately analyze and distinguish signals from background signals as taught by Lockhart et al (Column 23, line 41-Column 24, line 6).

R sponse to Arguments

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9. Applicant argues that Lockhart et al do not teach all the limitations of the claims i.e. random array and determining whether a discrete site contains a bead.

Applicant further argues that Walt et al do not teach all the limitations of the claims i.e. determining the similarity of a first signal at a discrete site with a reference signal and determining whether the discrete site contains a bead.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

However, as discussed above, it is acknowledged that Walt et al compare a first signal and second signal to determine bead presence (Column 19, lines 46-53) which clearly suggests that they compare the signal to a threshold signal (e.g. first signal) to determine presence of the bead. Additionally, Lockhart et al teach the missing element i.e. signal detection and comparison to a threshold measure. Lockhart et al further teach that their threshold comparison distinguishes a true signal from a background (Column 23, line 41-Column 24, line 6). As such, the combination of Walt et al and Lockhart et al teach all the limitations of the instant claims. Furthermore, Lockhart provides the motivation for applying their threshold comparison to the signal comparison of Walt i.e. to accurately analyze and distinguish signals from background signals as taught by Lockhart et al (Column 23, line 41-Column 24, line 6).

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29

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USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-4 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 49, 53 and 54 of copending Application No. 09/636,387 in view of Walt et al (U.S. Patent No. 6,327,410). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of determining the presence of a target analyte comprising acquiring a data image and differ only in the instant claims are drawn to mapping a grid onto the data image to create a registered data image. However, grid mapping (i.e. matrices) to provide a registered data image (optical signature) was well known in the art at the time the claimed invention was made as taught by Walt et al who teach that matrices-forming optical signatures facilitate comparison of optical signature and analyte detection (Column 19, lines 31-52). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the '387 method by mapping a grid onto the data image to create the registered data image for the expected benefit of facilitating analyte detection as suggested by Walt et al (Column 19, lines 47-53).

12. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

R sponse to Comm nts

13. Applicant's intention to file a Terminal Disclaimer upon indication of allowable subject matter is acknowledged.

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14. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878 until 13 January 2004. Starting 14 January 2004, the examiner's phone number will be (517) 272-0741. The examiner can normally be reached on 6:00 TO 3:30 Monday through Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
November 21, 2003